REMARKS

Status of the claims

Claims 3, 16-18 and 23 are in the case.

Priority

The present application claims priority on 60/448,883 as correctly noted by the Examiner. It does not however claim priority on Canadian application 2,410,153.

REJECTIONS UNDER 35 U.S.C. § 112, SECOND PARAGRAPH

Claims 3, 16-18 and 22 have been rejected under 35 U.S.C. § 112, second paragraph as being indefinite for failing to point out and distinctly claim the subject matter which the Applicant regards as the invention.

The Examiner alleges that it is not certain what is more than 97% identity to any fragment of Cry31Aa2.

Applicant traverses this objection as follows.

Claim 3 now reads:

"An isolated Cry31Aa polypeptide having cytotoxic activity against human cancer cells selected from the group consisting of Hela, Sawano, TCS, MOLT-4, HL-60, Jurkat, A549, Hep-G2 and Caco-2 cells, the polypeptide comprising a sequence having at least 97% identity with the amino acid sequence of SEQ ID NO: 8."

Claim 3 as amended clarifies that the isolated polypeptide comprises a sequence having at least 97% identity with the amino acid sequence of SEQ ID NO:8.

Applicant thus respectfully requests reconsideration and withdrawal of this rejection.

The Examiner also alleges that "[c]laim 17 is indefinite, because SEQ ID NO:15 is either Cry31Aa1 or Cry31Aa2. With the limitation in claim 3, which excludes positions 232-723 of SEQ ID NO: 18, it is concluded that SEQ ID NO:15 has to be

Cry31Aa2, which is the SEQ ID NO:8. Thus the claim is not further limiting". The Examiner also alleges that "[c]laim 16, 18 and 22 are included in this rejection because they depend from independent claim 3 and do not cure the deficiencies of claim 3".

Applicant respectfully traverses this objection as follows.

Claim 16 was reformulated into an independent claim and reads:

"An isolated Cry31Aa polypeptide having cytotoxic activity against human cancer cells selected from the group consisting of Hela, Sawano, TCS, MOLT-4, HL-60, Jurkat, A549, Hep-G2 and Caco-2 cells, wherein said polypeptide comprises the amino acid sequence of SEQ ID NO: 13, with the proviso that the polypeptide does not comprise amino acids 232 to 723 of SEQ ID NO: 18."

Claim 17 was made dependent on claim 16 and reads:

"The isolated polypeptide of claim 16, wherein said polypeptide comprises the amino acid sequence of SEQ ID NO: 15."

Applicant agrees that both 232-723 of SEQ ID NO: 18 (i.e. a fragment of Cry31Aa1) and activated Cry31Aa2 (i.e. SEQ ID NO: 8) satisfy SEQ ID NO: 15. Applicant however submits that SEQ ID NO: 15 is not limited to these two sequences. For instance, and as may be seen in the Sequence Listing of the instant application, SEQ ID NO: 15 encompasses a sequence that has an isoleucine at position 1 and an arginine at position 139. Such a sequence does not correspond to either of Cry31Aa1 (i.e. SEQ ID NO: 18) or activated Cry31Aa2 (i.e. SEQ ID NO: 8) since the former has a methionine at position 1 (i.e. corresponding to position 232 in SEQ ID NO: 18) and since the latter has a lysine at position 139 (i.e. also corresponding to position 139 in SEQ ID NO: 8).

Applicant thus respectfully requests reconsideration and withdrawal of this rejection.

REJECTIONS UNDER 35 U.S.C. § 102(b)

Claims 3, 16-18 and 22 are rejected as being anticipated by Mizuki et al. ("Mizuki") under 35 U.S.C. § 102(b).

The Examiner states that "[t]he instant invention claims different fragments of Cry31Aa, Cry31Aa1 and Cry31Aa2 that have cytotoxic activity against human cancer cells. On page 33, paragraph [0087] of the specification, Applicants state that cytocidal activity of the Cry31Aa1 was due to the cleavage by proteinase K and trypsin (Mizuki et al., 2000). Further, the specification states that the amino acids at positions 24, 37, 39, 51 and so on, see paragraph [0087] can be replaced by any other amino acid without abrogating the cytotoxicity of the protein that it constitutes against at least some cancer cells." And "[a]nalogously, Figure 5 of the instant invention, depicts SEQ ID NO:8 that contains different fragments showed also as Blocks 1-5, that are identical with these taught on page 629, Figure 4 of Mizuki et al. Further, in the instant invention, SEQ ID NO: 8 depicts trypsin activated Cry31Aa2. Therefore, any fragment of the CryAa protein being claimed in claim 3, would have to have more than 98% identity to biologically active fragments, where the biologically active fragments are not active unless clipped, as taught in Mizuki et al."

Applicants respectfully traverse the rejection as follows.

It is first submitted that the instant invention does not claim Cry31Aa1. CryAa1 is the polypeptide disclosed at Figure 3 of Mizuki *et al.* Cry31Aa1 is also presented as SEQ ID NO: 18 in the present application.

In her notes regarding art of interest no. 2 at page 6 of the instant Office Action, the Examiner states that: "96.6% identity to the SEQ ID NO: 8 is disclosed in Mizuki et al., "Parasporin, a human leukemic cell-recognizing parasporal protein of Bacillus thuringiensis, "Clin. Diagn. Lab. Immunol. 7:625-634 (2000)." This Mizuki *et al.* reference is the Mizuki publication cited by the Examiner in the present rejection.

Now, the instant invention recites in amended claim 3:

"An isolated Cry31Aa polypeptide having cytotoxic activity against human cancer cells selected from the group consisting of Hela, Sawano, TCS, MOLT-4, HL-60, Jurkat, A549, Hep-G2 and Caco-2 cells, the polypeptide comprising a sequence having at least 97% identity with the amino acid sequence of SEQ ID NO: 8."

Since Mizuki has less than 97% identity with SEQ ID NO: 8, while claim 3 recites a polypeptide comprising a sequence having at least 97% identity with the amino acid sequence of SEQ ID NO: 8, Mizuki does not anticipate claim 3 nor any of its dependent claims 18 and 23.

The instant invention also recites in claim 16:

"An isolated Cry31Aa polypeptide having cytotoxic activity against human cancer cells selected from the group consisting of Hela, Sawano, TCS, MOLT-4, HL-60, Jurkat, A549, Hep-G2 and Caco-2 cells, wherein said polypeptide comprises the amino acid sequence of SEQ ID NO: 13, with the proviso that the polypeptide does not comprise amino acids 232 to 723 of SEQ ID NO: 18."

As indicated earlier, SEQ ID NO:18 of the instant application is the sequence disclosed by Mizuki (see Figure 3 at page 628 of Mizuki). This sequence has since been officially designated Cry31Aa1. In the Mizuki reference, it was called parasporin.

SEQ ID NO: 13 of the instant application is a consensus sequence derived from an alignment of the activated Cry31Aa2 sequence of the present invention (i.e. SEQ ID NO: 8) with the fragment of Cry31Aa1 that corresponds to it, namely amino acids 232 to 723 of SEQ ID NO: 18. This alignment is presented in Figure 5 of the instant application.

Claim 16 expressly excludes from its scope any polypeptide comprising amino acids 232 to 723 of SEQ ID NO: 18. Hence, claim 16 expressly excludes from its

scope the sequence disclosed by Mizuki and a fragment thereof comprising amino acids 232 to 723 of SEQ ID NO: 18 and is thus not anticipated by this reference.

Applicant thus respectfully requests reconsideration and withdrawal of the rejection.

REJECTIONS UNDER 35 U.S.C. § 112, FIRST PARAGRAPH

Claims 3 and 16-18 and 22 are rejected under 35 U.S.C. § 112, first paragraph as failing to comply with the written description requirement.

The Examiner states that "[i]n claim 3, Applicants refer to an isolated Cry31Aa polypeptide fragment that comprises a sequence having at least 97% identity (an undefined fragment according to Examiner) with the Cry31Aa2 polypeptide fragment where the polypeptide does not consist of the Cry31Aa1 amino acid sequence fragment as set forth at positions 232 to 723 of SEQ ID NO:18. Examiner reviewed the specification for the support of claim 3, as currently amended, where different fragments of the polypeptide are claims, and Examiner did not find any support in the specification for the different fragments claimed in claim 3. Therefore amended claim 3 contains a new matter that is not supported in the specification as originally filed."

Claim 3 now reads as follows:

"An isolated Cry31Aa polypeptide having cytotoxic activity against human cancer cells selected from the group consisting of Hela, Sawano, TCS, MOLT-4, HL-60, Jurkat, A549, Hep-G2 and Caco-2 cells, the polypeptide comprising a sequence having at least 97% identity with the amino acid sequence of SEQ ID NO: 8."

Amended claim 3 does not include the objected "fragment" wording. Applicant respectfully submits that amended claim 3 fully complies with the written description requirement.

Applicant thus respectfully requests reconsideration and withdrawal of the rejection.

Examiner's notes regarding art of interest

The Examiner notes that "100% identity to the SEQ ID NO:8 is disclosed in Jung et al., "83-kDa crystal protein gene from a novel autoagglutinable, nonserotypeable strain of bacillus thuringiensis," Submitted February 2002 to the EMBL/GenBank/DDBJ databases."

Although Applicant understands that this note does not constitute a rejection *per* se in the present Office Action, Applicant wishes to submit the following to remove this reference as citable art any time in the future.

The Examiner is thus referred to the enclosed Declaration under 37 CFR 1.132 (Ex parte Magner) showing that Jung *et al.* is describing the Applicant's own work. Furthermore, as was also indicated in Applicant's response to the Office Action mailed November 3, 2005, Jung *et al.* was submitted to GenBank™ on 21 February 2002 under a confidentiality agreement. Pursuant to the Applicant's instructions, it was not published before 14 August 2004, namely after the filing of the present application.

The rejections of the claims are believed to have been overcome by the present remarks. From the foregoing, further and favorable action in the form of a Notice of Allowance is believed to be next in order, and such an action is earnestly solicited.

Examiner Rooke is invited to telephone the undersigned to discuss any remaining issues.